REMARKS/ARGUMENTS

Claims 1, 4, 6-7, 11-12, and 14-60 constitute the pending claims in this application. Claims 15-52 are withdrawn from consideration as being drawn to a non-elected invention. Applicants will cancel these claims upon indication of allowable subject matter in the elected invention. Claims 2-3, 5, 8-10, and 13 have been canceled without prejudice. Claims 53-60 have been added. Claims 1-2 and 6-13 have been amended. No new matter is being introduced. Applicants submit that the amendments and the new claims are fully supported by the specification and the original claims. The amendments are made solely to expedite prosecution of the application, and Applicants reserve the right to prosecute claims of similar or differing scope in subsequent applications.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Applicants note with appreciation that the amendments put forth in Paper No. 20 have been entered in full.

Applicants note with appreciation that the previous rejection under 35 U.S.C. 102 has been withdrawn.

Claim rejections under 35 U.S.C. 112, first paragraph

Claims 1-6 and 9-14 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants traverse this rejection to the extent that it is maintained over the amended claims.

Particularly, the Office Action asserts that these claims are "directed to methods employing biglycan or a protein having an amino acid sequence with 80%, 90% or 95% identity to SEQ ID NO: 9, or a portion of biglycan and possessing DAPC-stabilizing

stability. However, the instant specification fails to describe the entire genus of proteins, which are encompassed by these claims." The Office Action further alleges that the previous amendment of claim 1 ("being at least 80%, 90% or 95% identity to SEQ ID NO: 9, or a portion of biglycan and possessing DAPC-stabilizing stability") does not satisfy written description of physical or chemical characteristics of the proteins utilized in the claimed method.

Applicants submit that, pursuant to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, §1, "[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus."

Although, for the reasons already made of record, Applicants maintain that the claims comply with the written description requirement without amendment, Applicants have amended independent claim 1 and added new independent claim 53 which recites the subject matter of original claim 1, solely to secure rapid allowance of claims directed to commercially relevant subject matter.

As amended, claims 1 and 53 satisfy the written description requirement. For example, the claims recite functional characteristics coupled with a known or disclosed correlation between function and structure.

Claim 1 satisfies the written description requirement.

Amended claim 1 defines the biglycan polypeptide as "[comprising] a sequence at least 95% identical to amino acids 38-365 of SEQ ID NO: 9, wherein the polypeptide binds to alpha-dystroglycan and wherein the polypeptide comprises glycosaminoglycan (GAG) side chains." The claim is amended so as to place the claims in better condition for allowance, in compliance with 37 C.F.R. 1.116. Applicants submit that these

identifying characteristics have been presented in original claim 3 (e.g., "binding to alpha-dystroglycan") and in original claim 9 (e.g., "comprising glycosaminoglycan (GAG) side chains"). Support for the "95%" identity to mature bigylcan (e.g., amino acids 38-365 of SEQ ID NO: 9) can be found, for example, in original claim 11. Accordingly, the amendments hereby involve moving claim elements from formerly dependent claims into independent claim 1.

In addition, the specification amply teaches that both human biglycan and a torpedo biglycan ortholog (DAG-125) can bind to alpha-dystroglycan (see, e.g., Examples 1-5; pages 67-75). The specification further teaches that glycosaminoglycan side chains (e.g., chondroitin sulfate) are involved in binding of the biglycan to alpha-dystroglycan (see, e.g., Example 5; page 73, line 1 through page 75, line 10). In particular, the specification provides the domain structure of human biglycan which depicts two chondroitin sulfate attachment sites at the amino terminal region of the polypeptide (see, e.g., page 72, lines 24-29; and Figure 5C). Accordingly, the specification provides both working examples and sufficient description of these functional characteristics that are coupled with correlation between function and structure of the biglycan polypeptide. Based on the teachings of the specification, one of skill in the art would immediately visualize a wide spectrum of sequence and glycosylation variants that would bind to dystroglycan. One skilled in the art would reasonably conclude that Applicants had possession of the invention as claimed in claim 1.

Claim 53 satisfies the written description requirement

New claim 53 defines the biglycan polypeptide as "selected from the group consisting of: (a) a polypeptide comprising a sequence at least 95% identical to amino aids 38-365 of SEQ ID NO: 9 and capable of binding to alpha-sarcoglycan and gamma-sarcoglycan; and (b) a polypeptide comprising a sequence identical to SEQ ID NO: 9." The claims are amended so as to place the claims in better condition for allowance, in compliance with 37 CFR 1.116. Applicants submit that these identifying characteristics have been presented in original claim 4 (e.g., "binding to alpha-sarcoglycan and gamma-sarcoglycan"). Support for the "95%" identity to mature biglycan (e.g., amino acids 38-

365) of SEQ ID NO: 9 can be found, for example, in original claim 11. Accordingly, the amendments hereby involve moving claim elements from formerly dependent claims into independent claim 1.

In addition, the specification amply teaches that the biglycan can bind to alpha-sarcoglycan and gamma-sarcoglycan (see, e.g., Examples 6; page 75, line 12 through page 76, line 26). The specification further teaches that the biglycan binds to sarcoglycans via its core peptide (without glycosylation side chains) (see, e.g., page 75, line 12 through page 76, line 10). In particular, the specification teaches that the first 30 amino acids of human biglycan (cystein rich domain) can mediate binding of the biglycan to sarcoglycans (see, e.g., page 75, lines 16-22; page 76, lines 13-16). Accordingly, the specification provides both working examples and sufficient description of these functional characteristics that are coupled with correlation between function and structure of the biglycan polypeptide. Based on the teachings in the specification, one of skill in the art would be able to visualize biglycan variants possessing sarcoglycan binding, including essentially any variant possessing an N-terminal portion identical to or substantially similar to that of human bigylcan. One skilled in the art would reasonably conclude that Applicants had possession of the invention as claimed in claim 53.

For the reasons presented above, Applicants submit that all pending claims as amended fully comply with the written description requirement. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. 112, first paragraph, is respectfully requested.

Claim rejections under 35 U.S.C. 112, second paragraph

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. To expedite prosecution, Applicants have amended the claims to incorporate the Examiner's suggestions. Such amendments are not made in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope.

Specifically, the Office Action asserts that claims 1 and 12-14 are vague and indefinite due to the use of the term "biglycan" as a limitation. Solely to expedite prosecution, Applicants have amended the claims by removing the term "biglycan" to overcome the rejection.

The Office Action further points out that claims 1 and 2 include recitation of "or a portion thereof." It is not clear to the Examiner if a portion of biglycan or a portion of SEQ ID NO: 9. Applicants have amended the claims by removing the term "portion,".

The Office Action asserts that claim 13 is vague and indefinite for the recitation of "the biglycan comprises the amino acid sequences of SEQ ID NOs: 1-3." Applicants have canceled claim 13, rendering the rejection moot.

The Office Action asserts that claims 2-11 are indefinite for being dependent from the indefinite claim. Applicants have amended independent claim 1, thereby rendering this rejection moot.

Based on the above arguments, Applicants submit that all claims as amended comply with the requirement of 35 U.S.C. 112, second paragraph. Therefore, reconsideration and withdrawal of rejections under 35 U.S.C. 112, second paragraph, is respectfully requested.

Claim rejections under 35 U.S.C. 103(a)

Claims 7-8, 10-11, and 13-14 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ruoslahti et al. Specifically, the Office Action asserts that "one skilled in the art, by reading the disclosure of Ruoslahti et al. which clearly employs a method of contacting biglycan with a tissue, would reasonably expect that as long as molecule is identified as biglycan, regardless of its precise molecular structure, it can be successfully used in the protocol provided by Ruoslahti et al. By practicing the protocol of Ruoslahti et al., stabilizing of DAPCs on the surface of a cell is inherently achieved, absent evidence to the contrary." Applicants traverse this rejection in its entirety, but in the

interest of brevity, Applicants' rebuttal is limited to the rejection to the extent that it is maintained over the amended claims.

As described above, Applicants have amended claim 1 to specify that the biglycan polypeptide comprises a sequence at least 95% identical to amino acids 38-365 of SEQ ID NO: 9, wherein the polypeptide binds to alpha-dystroglycan and wherein the polypeptide comprises glycosaminoglycan (GAG) side chains.

Applicants respectfully submit that Ruoslahti et al. fail to provide any structural characteristics of the biglycan in their methods. In particular, Ruoslahti et al. do not teach that the biglycan can bind to alpha-dystroglycan or the biglycan comprises glycosaminoglycan (GAG) side chains. In the absence of such teachings, one of skill in the art would not know if the biglycan of the Ruoslahti et al.'s method has the structural/functional properties as recited in claim 1. Further, Applicants submit that a skilled artisan would not have had a reasonable expectation of success even if the Ruoslahti reference were combined with a specific biglycan sequence. As a matter of fact, Applicants have found that all biglycans do not bind α-dystroglycans equally well. For example, "biglycan purified from articular cartilage bound α-dystroglycan poorly" (see, e.g., page 75, lines 4-7).

As described above, Applicants have added new claim 53 that recites certain embodiments of original claim 1. Claim 53 specifies that the cell is a muscle cell and that the biglycan polypeptide is selected from the group consisting of: (a) a polypeptide comprising a sequence at least 95% identical to amino acids 38-365 of SEQ ID NO: 9 and capable of binding to alpha-sarcoglycan and gamma-sarcoglycan; and (b) a polypeptide comprising a sequence identical to SEQ ID NO: 9.

Applicants respectfully submit that Ruoslahti et al. fail to teach the use of a biglycan in a muscle cell. Ruoslahti et al. merely describe that the tissue is related to a pathology which is fibrotic cancer, fibrosis of the lungs, arteriosclerosis, post myocardial infarction, glomerulonephritis, cardiac fibrosis, post-angioplasty restenosis, renal interstitial fibrosis, scarring or a diabetes-associated pathology. Notably, although the

Ruoslahti et al. reference describes multiple different tissues and pathologies, it fails to describe the muscle. Further, Applicants submit that Ruoslahti et al. fail to provide any structural characteristics of the biglycan in their methods. In particular, Ruoslahti et al. do not teach that the biglycan can bind to alpha-sarcoglycan and gamma-sarcoglycan. In the absence of such teachings, one of skill in the art would not know if the biglycan of the Ruoslahti et al.'s method has the structural/functional properties as recited in claim 53. In addition, a skilled artisan would not have had a reasonable expectation of success even if the Ruoslahti reference were combined with a specific biglycan sequence. Ruoslahti et al. at most suggest that the biglycan suppresses the extracellular matrix producing activity of TGF-β in tissues under certain pathological conditions as described above. However, the reference offers no clue as to whether the biglycan bind to alpha-sarcoglycan and gamma-sarcoglycan in a muscle cell.

Pursuant to MPEP 2143, "[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations."

Accordingly, Applicants submit that at least two of the three requirements for establishing a *prima facie* case of obviousness is missing, reconsideration and withdrawal of rejection under 35 U.S.C. 103(a) is respectfully requested.

CONCLUSION

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims are now in condition for allowance and early notification to this effect is earnestly solicited. Any questions arising from this submission may be directed to the undersigned at (617) 951-7000.

If there are any other fees due in connection with the filing of this submission, please charge the fees to our **Deposit Account No. 18-1945.** If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit account.

Respectfully Submitted,

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